Remarks

The present invention is directed to methods of delaying or reducing the progression of Alzheimer's disease. Claims 1-18 have been cancelled. Claims 19-27 are currently pending.Claim 19 has been amended. Claims 21 and 22 are withdrawn from consideration.

Rejections under 35 U.S.C. 112 second paragraph

Claims 19, 20 and 23-27 are rejected under 35 U.S.C. 112 second paragraph, as being indefinite. Applicants respectfully traverse this rejection as it applies to the amended claims.

The Examiner objects to the term "antigenic peptide" for lacking antecedent support. Claim 19 has been amended to provide proper antecedent support for this term. Withdrawal of this rejection is respectfully requested.

The Examiner also asserts that the term "supramolecular antigenic construct" is not adequately defined in the specification, and is therefore unclear. Applicants respectfully traverse this rejection and refer to page 20, line 23 to page 21, lines 11 of the specification where a clear definition of the phrase "supramolecular antigenic construct" is provided from which is it very clear that this term includes any antigenic peptides.

In particular, it is set forth in the 2nd last paragraph on page 20 that "The supramolecular antigenic constructs of the present invention generally comprise peptides modified to enhance antigenic effect wherein such peptides are modified via pegylation (using polyethylene glycol or modified polyethylene glycol), or modified via other methods such by palmitic acid, … … and the like."

It is only in a specific embodiment of the invention (as now claimed) that the term "supramolecular antigenic construct" is relating specifically to amyloid peptide. Reference is

made in this respect to lines 10 and 11 on page 21, where it is clarified that "In certain embodiments, the supramolecular antigenic constructs comprise a peptide having the amino acid sequence of β-amyloid."

The claims are interpreted in view of the teachings of the specification. One of ordinary skill would clearly understand the meaning of this term in view of the description in the specification. Applicants respectfully request withdrawal of this rejection.

Rejections under 35 U.S.C. 112 first paragraph (enablement)

Claims 19, 20 and 23-27 are rejected under 35 U.S.C. 112, first paragraph, because the Examiner asserts that the specification does not reasonably provide enablement for methods of treating Alzheimer's disease. Specifically, the Examiner cites two articles that state that there is no treatment for the diseases described in the specification and that the Applicants have not provided any working examples.

Applicants respectfully note that the states that there exist five FDA-approved drugs to treat symptoms of Alzheimer's disease. However, in order to facilitate prosecution, Applicants have amended to claims to recite methods of "delaying or reversing the progression of Alzheimer's disease…" The Examiner agrees that treatments of symptoms exist and therefore this language should overcome this rejection. This amendment is supported at page 3, lines 30-33 of the specification where it states that treatments aimed at changing the underlying course, and thus delaying or reversing the progression of Alzheimer's disease have been largely unsuccessful. From this passage, the skilled person would understand that it was an objective of the present invention to change this unsatisfactory situation by providing a solution to the problem. Accordingly, it is set forth at page 5, lines 12-15 that what is needed is "effective

compositions an methods for addressing the complications associated with neurological disease associated with plaque formation such as Alzheimer's disease." Applicants respectfully request withdrawal of this rejection.

Rejections under 35 U.S.C. 112 first paragraph (written description)

Claims 19, 20 and 23-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The Examiner is objecting to the breadth of the claim scope by the term "supramolecular antigenic construct". To facilitate prosecution, Applicants have amended the claims to specify that the supramolecular antigenic construct includes "an antigenic peptide having the amino acid sequence of β-amyloid, or an active fragment thereof, wherein the antigenic peptide or active fragment is modified with hydrophobic moieties to enhance antigenicity." This language is found in the specification as filed at pages 15, and 20. Withdrawal of this rejection is respectfully requested.

Rejections under 35 U.S.C. 102(b)

Claims 19, 20 and 23-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Nicolau et al., PNAS, 2002 vol. 99, no. 4, p. 2332-2337 ("Nicolau"). Applicants respectfully traverse the rejection as it applies to the amended claims.

The Examiner asserts that Nicolau teaches methods of administering a palmitoylated SEQ ID NO:1 in a liposome carrier and asserts that Nicolau inherently treats Alzheimer's disease by administering this composition to a NORBA transgenic mouse. Applicants respectfully note

that the newly amended claim is directed to a method for delaying or reversing the progression of Alzheimer's disease. No such method is disclosed in Nicolau. Nicolau is only successful in treating pancreatic plaques in the NORBA mouse.

To the contrary, Nicolau express serious doubts as to the value of their NORBA mouse model in the treatment of Alzheimer's disease because the NORBA mouse model does not provide a blood-brain-barrier to cross for the antibodies to reach the pancreatic plaques (see page 2337, left col., 2nd paragraph). Nicolau fails to show any action of administering this compound on plaque deposition in the brain, or to reduce symptoms of Alzheimer's disease.

Furthermore, it is exactly this blood-brain-barrier which was considered one of the major obstacles for an immunization approach to be successful, because it was unpredictable before the present invention as to whether the antibodies produced as a result of the immunization process would be able to cross the blood-brain-barrier, and thus reach the plaques in the brain.

The only statement that Nicolau makes with respect to the treatment of Alzheimer's disease based on the pancreas data obtained through the use of their NORBA mouse model is that "Possible implications for the therapy of Alzheimer's disease are discussed." (Abstract). However, there is no such discussion found in Nicolau except a very general and speculative suggestion at the end of the paper that there may be a "possible therapeutic and a prophylactic role for vaccination with a chemically modified Aβ fragment reconstituted in a liposome." The only therapeutic or prophylactic role shown by Nicolau is the removal of plaques in the pancreas which has no blood-brain-barrier. Nicolau fails to anticipate methods for treating diseases where antibodies need to cross the blood-brain-barrier.

Contrary to the teachings of Nicolau, the present application provides a detailed description of the test to be carried out in order to determine the efficacy of antibodies elicited by

the methods described in the application, (by using supramolecular constructs as claimed, in terms of memory restoration (See Example at pages 38-40 of the specification)), and also clear evidence that significant levels of memory restoration and of curiosity awakening can be observed in a transgenic Alzheimer APP[V717] mouse model (see page 23, lines 19-21).

Applicants respectfully assert that the Examiner's application of the inherency standard is inconsistent with the case law. The Examiner's own Manual of Patent Examining Procedure (MPEP) states that "the discovery of a new use for an old structure based on unknown properties of the structure might be patentable to the discoverer as a process of using. *In re Hack*, 245 F.2d 246, 248, 114 USPQ 161, 163 (CCPA 1957).

In the present application, the claimed method of delaying or reversing the progression of Alzheimer's disease is not merely a result or property of the composition. It is a novel method of administering the supramolecular constructs recited in the claimed methods to cross the blood-brain barrier and delay or reverse the progression of Alzheimer's disease. This is not disclosed by Nicolau explicitly or inherently. In fact, the efficacy of the antigenic constructs recited in the claims for delaying or reversing the progression of Alzheimer's disease was unexpected in view of the self-doubting statements by Nicolau at page 2337. Nicolau did not disclose the claimed methods, and even discouraged others from attempting these methods.

The evidence in the present specification is confirmed and supported by data reported in Muhs et al (2007), (enclosed) which shows that immunization of a transgenic Alzheimer mouse model creates antibodies that cross the blood brain barrier, and that are useful for treating plaque deposition in the brain that leads to a significant increase of the cognitive memory capacity of the immunized mice in the object recognition test contrary to the negative teachings of Nicolau. (see page 9811, right col, last paragraph)

Applicants assert that Nicolau fails to anticipate a method for delaying or reversing the progression of Alzheimer's disease as claimed. Withdrawal of this rejection is respectfully requested.

Conclusions

Applicants submit that the response herein provides a complete response to the Office Action dated August 11, 2009.

If the Examiner believes there are other issues that may be resolved by telephone interview, or that there are any informalities remaining in the application that may be corrected by Examiner's Amendment, a telephone call to the undersigned is respectfully solicited.

No additional fees are believed due, however the Commissioner is hereby authorized to charge any additional fees that may be required, or credit any overpayment of fees to Deposit Account number 11-0980.

Respectfully submitted,

/Stephen C. MacDonald, Ph.D./
Stephen C. MacDonald, Ph.D.
Reg. No. 60,401

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King & Spalding LLP
1180 Peachtree Street
Atlanta, Georgia 30309-3521
404-572-2715 (telephone)
404-572-5135 (facsimile)